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*Review*

# Longevity and ageing: appraising the evolutionary consequences of growing old

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Senescence or ageing is an increase in mortality and/or decline in fertility with increasing age. Evolutionary theories predict that ageing or longevity evolves in response to patterns of extrinsic mortality or intrinsic damage. If ageing is viewed as the outcome of the processes of behaviour, growth and reproduction then it should be possible to predict mortality rate. Recent developments have shown that it is now possible to integrate these ecological and physiological processes and predict the shape of mortality trajectories. By drawing on the key exciting developments in the cellular, physiological and ecological process of longevity the evolutionary consequences of ageing are reviewed. In presenting these ideas an evolutionary demographic framework is used to argue how trade-offs in life-history strategies are important in the maintenance of variation in longevity within and between species. Evolutionary processes associated with longevity have an important role in explaining levels of biological diversity and speciation. In particular, the effects of life-history trait trade-offs in maintaining and promoting species diversity are explored. Such trade-offs can alleviate the effects of intense competition between species and promote species coexistence and diversification. These results have important implications for understanding a number of core ecological processes such as how species are divided among niches, how closely related species co-occur and the rules by which species assemble into food-webs. Theoretical work reveals that the proximate physiological processes are as important as the ecological factors in explaining the variation in the evolution of longevity. Possible future research challenges integrating work on the evolution and mechanisms of growing old are briefly discussed.

**Keywords:** ageing; evolutionary dynamics; longevity; mathematical models; population dynamics

## 1. INTRODUCTION

Senescence is a decline in physiological functioning that leads to a decrease in reproduction and an increase in mortality with age. Senescence appears maladaptive as it directly affects key life-history traits (such as the schedules of reproduction and survival) that influence fitness. It is an intriguing puzzle to evolutionary biologists. However, a fascination with ageing, extending life and even finding the elixir of life widely pervades human culture, extending beyond the field of evolutionary biology. Ancient Chinese iconography depicts Shou-lao (Shou-xing, Amitayus), the God of Longevity, with elixirs of immortality, and in Japanese mythology Jurojin (God of Longevity) is often depicted holding a scroll with the lifespan of all living things laid out. In Greek mythology, The Fates (Clotho, Lachesis and Atropos) determine the lifespan of man by mapping out the pattern or thread of life (Clotho), its length (Lachesis) and when it is cut (Atropos). Even Aristotle outlined an understanding for life, death and longevity.

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Given the popular appeal of ageing (Ricklefs & Finch 1995), it is of little surprise that gerontology is a diverse and stimulating branch of the natural sciences. Questions on the biology of ageing range from the molecular through to the whole organism- and population-level, and from the pathological (exploring how the existence of free radicals, the by-products of cellular metabolism, affect disease progression and ageing) through to evolution (exploring why fundamental variability in longevity exists). Although, the general theory for the evolution of senescence is well established (Medawar 1952; Williams 1957; Hamilton 1966), the necessity for 'improvement is long overdue' (Williams 1992). To quote Williams (1992) further: a fuller theory of the evolution of senescence should be a 'fitness-maximization model with realistic genetic, development and demographic constraints. It must be able to predict the effects of age on measures of adaptive performance in a diversity of populations subject to senescence'.

The main goal in this article is to review and develop theory on this issue. Specifically, the objective is to explore how the processes of demography and physiology (evolutionary demography) coupled with natural selection shape ageing, and examine the consequences of selection on this life-history characteristic for species diversity and diversification.

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Table 1. Glossary of definitions and terms.

| | |
|---|---|
| ageing | a decline in an organism's fertility or survival though time |
| apoptosis | cell death induced by molecular mechanism of ageing |
| evolutionary stable | strategy uninvadable by any other |
| fitness | a measure of the spread of gene into future generations |
| free radicals | the reactive by-products of cellular metabolism |
| gene environment effect | genotypes respond differently in different environments |
| gerontology | the study of ageing |
| hazard of mortality | probability of dying within an interval of time |
| lifespan | the period of life from birth until death |
| pleiotropy | the multiple phenotypic effects of a gene |
| population dynamics | change in the size of the population through time |
| senescence | a progressive increase in the age-specific death rate (also see *ageing*) |
| trade-off | constraints on resource allocation patterns |
| statistical distribution | number of times each possible outcome occurs in a number of trials |

To begin, and focus the thoughts and ideas presented, we introduce an iconic representation: the Darwinian demon. This mythical entity is an organism that grows quickly, breeds fast, outcompetes all and never ages. In this article, we will explore why this life history cannot persist and, thus, why such an organism does not exist. We will show how trade-offs between survival and mortality arise and influence Darwinian fitness. The article begins with a wide-ranging overview of the biology of ageing, including the molecular mechanisms and evolutionary theories of ageing. Although much of this material may have been reviewed elsewhere, it provides a robust point of departure for understanding why the mechanisms determining evolutionary demography are central to the evolution of ageing. The role of physiological complexity on the evolutionary consequences of longevity is then explored. Here, it is shown how the evolution of physiological complexity can determine and influence mortality rates. Recent developments in understanding how heterogeneous mortality rates arise and can permit coexistence of different life-history strategies are considered. In §4, rather than reiterating existing hypotheses and thoughts, an overview of novel areas of research and future directions of the field are discussed. A glossary of terms and definitions used throughout the article is given in table 1, and details of the technical aspects of the article are given in the electronic supplementary material.

## 2. BIOLOGY OF AGEING

### (a) *Mechanisms of ageing*

While no single gene can be credited as responsible for ageing, the mechanisms of ageing are clearly under genetic control. The molecular, cellular and physiological aspects of ageing involve various forms of damage to DNA, cells, tissues and organs. This so called 'free radical theory of ageing', originally conceived by Harman (1956), provides a central theme in the biology of ageing. Harman (1956) hypothesized that endogenous oxygen radicals produced during aerobic respiration could cause cumulative oxidative damage resulting in senescence and eventual death (of cells, tissues and organs). Since its inception, this theory has attracted wide interest from a diverse range of studies. With the advent of molecular biology, analysis of the diversity of the action of oxygen derived free radicals has led this field of research to rapidly expand (Beckman & Ames 1998; Halliwell & Gutteridge 1999).

It is important, at the outset, to distinguish between the causes and consequences of ageing. For example, the accumulation of the end-products of oxidative damage (such as lipofuscin: a complex of lipid and protein residues) through changes in lysosome activity is thought to arise as a consequence of ageing (Beckman & Ames 1998) rather than as a cause of ageing. However, oxidative damage might accumulate with age. While certain 'biomarkers' of ageing suggest that net oxidative damage does not markedly increase with age (Halliwell & Gutteridge 1999), there is clear evidence that structural changes to proteins, and free radical production by mitochondria and muscle (Beckman & Ames 1998) do change with increasing age. This may even be a positive feedback loop in that damage to mitochondrial membranes and proteins can lead to the generation of more free radicals (Sohal & Sohal 1991).

The free radical theory of ageing is a molecular mechanism for the rate of living theory, initially explored by Loeb and colleagues (Loeb & Northrop 1916) and popularized by Pearl (1928). Using a detailed series of experiments with *Drosophila melanogaster*, Pearl's central theses were that physiological limitation determines the duration of life and that lifespan varies inversely with the rate of energy expenditure (the rate of living). The former of these suggests that between species differences exist in longevities based on physiological performance. This theme is developed in §3. The latter hypothesis suggests that the faster organisms burn fuel, the shorter their life expectancy.

Reducing calorie intake, for example, has been shown to slow ageing in a variety of organisms spanning all the major phyla including mammals (e.g. rodents, McCay *et al.* 1935; primates, Lane *et al.* 2001), invertebrates (e.g. spiders, Austad 1989; *Drosophila*, Partridge *et al.* 2005) and fungi (e.g. yeasts, Lin *et al.* 2004). However, the nematode, *Caenorhabditis elegans* has taken this phenomenon to another level. In response to high population density and/or reduced resource availability, larval nematodes arrest development at the third instar (the *dauer*) and can survive in this stage for at least 60 days (Klass & Hirsh 1976). As conditions improve, dauers moult and develop to

adulthood to reproduce normally. Rate of living effects correlate with a range of abiotic variables. For instance, in the rockfishes, longevity increases with maximum depth (Cailliet *et al.* 2001). Rockfishes (*Sebastes* spp.) are relatively sedentary, deeper depths are relatively colder and have low $O_2$ concentrations, and food resources are scarce: all of which suggest a decline in rockfish metabolic activity (rate of living) with depth. However, assessment of the rate of living might also be confounded with body mass (Promislow & Haselkorn 2002) since size, metabolic rate and longevity may be tightly linked (West *et al.* 2001). Disentangling this phenomenological effect on the processes of ageing still requires a degree of unequivocal resolution.

To reiterate, Harman's theory on the free radical damage (Harman 1956) is the molecular manifestation of the rate of living theory. Burning calories increases oxidative damage and results in shorter lifespans. Recently, molecular genetic studies have shown that calorie restriction is dependent on a few core molecular pathways (Koubova & Guarente 2003). Caloric restriction leads to a range of molecular, hormonal and cellular changes. The function of one gene, in particular, appears to have wide effects. Sir2 is a gene in yeast that regulates lifespan: in its absence the lifespan of *Saccharomyces cerevisiae* is shortened. Sir2p, the protein encoded by this gene, operates only in the presence of $NAD^+$ (rather than other cofactors such as NADH, $NADP^+$, or NADPH). In yeast, glucose-restricted diets increase respiration, increase $NAD^+$ conversion and potentially activate Sir2p (Koubova & Guarente 2003; Lin *et al.* 2004), leading to increased lifespan. This gene is highly conserved and is known to affect ageing across a broad range of organisms. A similar gene (sir-2.1) in *C. elegans* is thought also to increase longevity (Hekimi & Guarente 2003), while in mammals the activity of this gene affects cell apoptosis.

Studies on *C. elegans* suggest that hormones involved in glucose metabolism also influence ageing. Mutant worms with reduced functionality for detecting insulin (via the insulin/insulin growth factor (IGF)-1 pathway) live longer (Kenyon *et al.* 1993; Kimura *et al.* 1997). One model for the integration of the molecular, cellular and hormonal control of ageing again involves Sir2 proteins detecting calorie restriction as a change in $NAD^+$ levels. More $NAD^+$ leads to downregulation of insulin and an increase in lifespan by reducing cell apoptosis and other cellular metabolic processes (Koubova & Guarente 2003).

One major process which reduces the impact of oxidative damage is the function and action of antioxidants. Antioxidant defences include enzymes that remove free radicals (including peroxidase and superoxide dismutase (SOD)), proteins that reduce the availability of pro-oxidants such as iron (such as metallothionein) and free radical scavengers (such as Vitamin C (ascorbic acid) and Vitamin E (tocopherols); Halliwell & Gutteridge 1999). Antioxidants such as SOD are widespread across all taxa and their role in reducing oxygen toxicity is undoubted. However, their role in reducing mortality rates and extending lifespan is more questionable. By engineering *Drosophila* to express more SOD and catalase, Sohal & Weindruch (1996) illustrated that these enzymes can decrease fly mortality rates. Interpretation of these effects, however, should be viewed with caution (Orr & Sohal 2003) as they may more realistically reflect differences in underlying genetic background rather than species specific responses to changes in antioxidant levels. More specifically, it has been shown that the expression of SOD is not necessarily a prerequisite for the evolution of long lifespans (Parker *et al.* 2004). Using the ant, *Lasius niger*, Parker *et al.* (2004) showed that the longevity differences between queens (>28 years), workers (1–2 years) and males (weeks) is not associated with the over-expression of antioxidants such as SOD.

The accumulated deterioration of mitochondria is a further consequence of oxidative damage (Miquel 1998). Postmitotic cell ageing is, as discussed, influenced by metabolic rate. However, Miquel and colleagues (Miquel *et al.* 1980; Miquel 1991, 1992) have proposed a theory of ageing based on oxygen toxicity and age-related mitochondria dysfunction. Extranuclear, somatic gene mutations in mitochondrial DNA (mtDNA) are correlated with the production of oxygen free radicals. As mtDNA is unable to prevent this intrinsic damage (as it lacks excision and repair processes), the resulting mitochondrial impairment and subsequent decline in cellular energy function leads to cell death and ageing (or age-related syndromes such as disease). With this mitochondrial theory of ageing, it is important to bear in mind that processes of irreversible cell differentiation and chronic oxygen stress underpin cellular ageing and, consequently, observable senescence.

It is important to appreciate that oxygen, its toxicity and metabolism lead to cell damage, senescence and apoptosis in all these mechanisms (Lane 2002). When damage ensues, molecular machinery within the cells acts to limit this damage. In cells, for example, damage to DNA due to oxidative processes causes the upregulation of a protein called p53. This protein halts the cell cycle in the G1 phase and induces cell death. If a cell has mutant versions of p53, it can live on potentially forever. Understanding how this protein operates is essential in understanding the biology of benign and malignant cancer growths. It is now well established that normal cells have a limited capacity to divide. This phenomenon is known as the 'Hayflick limit' (Hayflick 1965; Shay & Wright 2000). Early evolutionary biologists, such as August Weissman, argued that death occurs as tissue cannot continue renewing forever, as there are limits on cell division (Weismann 1889). However, it was another 80 years before this idea was proved. Against conventional thinking and with a remarkable set of experiments, Hayflick & Moorhead (1961) demonstrated that there was a limit to the number of divisions of normal cells (compared to tumour cells, which are immortal). This counting mechanism has two broad implications. The first is that cells can only undergo a fixed number of divisions, and a second even more fascinating implication is that cryogenically preserved cells 'remember' how many divisions they have made (so while cryogenic preservation may be advantageous in the short term, there still remains a finite limit to life).

The importance of the Hayflick limit for understanding the mechanisms of ageing was discovered by Olovnikov (1973, 1996). Olovnikov understood that the properties of DNA replication prevent cells from fully transcribing the ends (telomeres) of nuclear DNA. By appreciating that repeated division of cells shortens DNA, Olovnikov found a molecular mechanism to explain the Hayflick limit. Neoplastic growths solve the telomere problem by using telomerase, an enzyme that synthesizes and elongates telomeres (Greider & Blackburn 1985), and so avoid the inevitability of the Hayflick limit.

Recently, the role of telomere length on ageing in organisms has been debated. Telomeres are highly conserved regions of DNA (Ridley 1999) and the effects of telomere shortening have been shown to be correlated with lifespan in birds and mammals (Haussmann *et al.* 2003, 2004). By sampling bone marrow and erythrocytes from birds with markedly different lifespans, species with shorter lifespans were shown to lose more telomere repeats as they age than species with longer lifespans. Similar correlations were also recorded for mammals (Haussmann *et al.* 2003). However, more recently, the positive correlation between telomere attrition and longevity has been shown to be confounded by body size (Hall *et al.* 2004). In two long-lived seabirds (the shag and the wandering albatross), substantial between-individual variation in the magnitude of telomere loss was recorded and individuals laying down more tissue mass for their size showed greater telomere shortening (Hall *et al.* 2004). So while telomeres are a molecular manifestation of the Hayflick limit, there remains the potential for developing more inclusive theory that links this molecular machinery to the processes of ageing and longevity.

Unlike clonal senescence as observed by Hayflick's fibroblasts lines (where all cells die at approximately the same age), it has been shown more recently that the process of cell division in many organisms which give rise to new offspring is asymmetric. That is, there is a distinction between parent and daughter cells, with differential molecular processes affecting development and ageing between these cell types. During cell division or budding in the yeast *S. cerevisiae*, enlarged mother cells are readily distinguishable from smaller daughter cells. Using this morphological characteristic, Mortimer & Johnston (1959) first demonstrated that *S. cerevisiae* undergoes replicative senescence with individual cells dying after about 20 divisions. More recently in the fission yeast *Schizosaccharomyces pombe* it has been shown that the processes of cell division are also asymmetric (Barker & Walmsley 1999), leading to individual cells dying after about 15 divisions. In organisms that undergo morphologically symmetric divisions similar processes might also lead to cell ageing and death. In *Escherichia coli*, ageing has recently been shown to be related to the inheritance of pole cells (the end of the cell). Bacteria that inherit the old pole cell (as the rod-shaped *E. coli* divides from the middle) grow more slowly, produce offspring with less biomass and have an increased probability of dying (Stewart *et al.* 2005).

Appreciating this evidence for the molecular mechanisms of ageing is essential. For once these processes are understood, then the rate of ageing or lifespan could be determined. However, these details on the mechanistic view of ageing raise two questions. First, is it appropriate to define lifespan or rate of ageing as a measure of longevity? Second, is it sufficient knowing the mechanisms of ageing to argue that the process of growing old is inevitable?

(i) *Is it appropriate to define lifespan as a measure of longevity?*

While this might be perceived as a semantic issue, understanding measures of longevity is essential if the evolutionary, biodemographic or gerontological aspects of ageing are to be properly understood. It has been known for almost two centuries that age-related mortality trajectories follow an exponential increase (Gompertz 1825)

$$\mu(a) = A + C\exp(Ga), \tag{2.1}$$

where $\mu(a)$ is the mortality rate at age $a$, $A$ is the constant extrinsic mortality, $C$ is the constant intrinsic mortality and $G$ is the actuarial ageing rate. On a logarithmic scale, $G$ is often cited as a measure for the rate of ageing (e.g. Carey 2001). Although the Gompertz relationship might be appropriate as a measure of ageing under a range of different scenarios (Easton 1995; Kowald 2002), it fails to account for (genetic) heterogeneity that might give rise to nonlinear mortality trajectories (Carey *et al.* 1992; Carey 2003; Mangel & Bonsall 2004). The Gompertz model (equation (2.1)) shows that mortality depends on three processes: extrinsic mortality, intrinsic susceptibility and the actuarial ageing rate. By definition, lifespan is also a function of these processes (Kowald 2002) and it is then not appropriate to conflate ageing with lifespan, since differences in vulnerability and ageing rate interact to determine mean lifespan. However, appreciating that lifespan combines a range of biological and environmental processes suggests that this is an appropriate measure of longevity.

(ii) *Is it sufficient knowing the mechanisms of ageing to argue that the process of growing old is inevitable?*

Many organisms show determinate patterns of growth: i.e. organisms reach a fixed size at sexual maturity. Age-related dysfunction emerges after the onset of reproduction, although this need not be a gradual accumulation of loss of function (Finch 1990). Examining broad taxonomic patterns suggests wide variation in longevities. Comfort (1979) records at least 25 species of birds that have lifespans of more than 40 years. Comparing species of similar body size reveals remarkable variability in longevities: e.g. bats live three to fivefold longer than rodents, parasitic wasps (figure 1*a*) which attack the same host show marked variability in survival (Bonsall *et al.* 2002) and, similarly, molluscs (an invertebrate phylum of over 130 000 species) show patterns of senescence varying from centuries (e.g. clams) to months (e.g. sea hares; Finch 1990).

In contrast, some organisms show indeterminate patterns of growth, where growth continues after reaching sexual maturity. These organisms tend to show no patterns of age-related dysfunction and

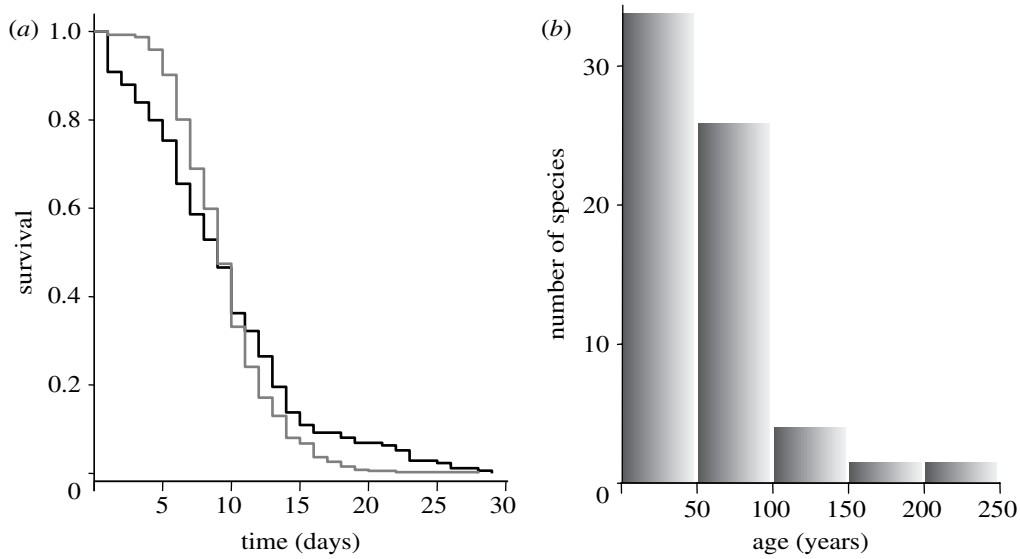


Figure 1. Patterns of mortality and lifespan. (*a*) Survival curves for *Leptopilina heterotoma* (black line) and *Asobara tabida* (grey line), parasitic wasps (natural enemies) of *Drosophila subobscura*. Note that *Leptopilina* shows much more variability in survival than *Asobara* (from Bonsall *et al.* 2002). (*b*) Histogram of recorded lifespans for 55 species of rockfish (*Sebastes* spp.; data compiled from Love *et al.* 2002).

age-dependent mortalities that are constant following sexual maturity. Organisms showing indeterminate growth span a variety of taxonomic groups. The rockfishes (figure 1*b*), for example, show variability in longevity spanning at least one, if not two, orders of magnitude. Some species live for 8–10 years, others (even accounting for sources of error) live for over 150 years. Vascular plants such as the famous redwoods (*Sequoia sempervirens*, *Sequoiadendron giganteum*), the Australian tropical Bumpy Satinash (*Syzygium cormiflorum*, a spectacular tree, which flowers along its trunk) and the favourite of English churchyards, yew (*Taxus baccata*), all show extensive and extended patterns of longevity. Parenthetically, the longevity of *T. baccata* features in Gilbert White's writings: 'it seems to have seen several centuries, and is probably coeval with the church' *Letter V: The Antiquities of Selborne* (White 1789). This famous tree, in the churchyard at Selborne, was estimated to be over 1400 years old, when it succumbed to the vagaries of the British climate (dying from extrinsic mortality rather than intrinsic processes).

All of this suggests that even though, the mechanisms of ageing are under genetic control, the manifestations of senescence are as different as the difference between species. So, even if the proximate causes of ageing are understood and appreciated, the underlying evolutionary processes necessary to interpret the diversity and variability in this life-history trait still require explanation. More succinctly, it is important to draw distinction between the 'private' mechanisms (those confined to a particular species or groups of related species) and the 'public mechanisms' (such as oxidative damage) of ageing (Martin *et al.* 1996; Partridge & Gems 2002) within an evolutionary framework.

### (b) *Why isn't it optimal to live forever?*

A group-selectionist argument would suggest that finite lifespans or ageing has evolved to benefit a group, society or species by removing elderly individuals and maximizing the benefits of more resources to the group. While it might appear that there is some merit in these arguments, here we will explore why selection at the individual level is likely to be more predominant.

Weismann (1889) first noted that a distinction should be drawn between the evolutionary and physiological approaches associated with ageing; the former focus on why ageing evolves and the latter concentrate on how ageing occurs. However, Weismann proposed a group-selection argument as a solution to the issue of ageing. Little further progress was made on the evolutionary approaches to ageing for another 60 years until Medawar (1952) argued that the force of natural selection that maintains individual survival and fertility declines with increasing age. Medawar suggested that mutations acting early in life would be eliminated by natural selection. However, mutations that appeared at or around reproductive maturity would not be purged by natural selection (Partridge & Barton 1993), could accumulate and lead to a decline in survival and/or fertility. This is the so-called *mutation accumulation theory of senescence* (Medawar 1952).

Using the Euler–Lotka equation

$$\sum_{a=1}^{\alpha} \mathrm{e}^{-ra} l(a) m(a) = 1, \tag{2.2}$$

where $l(a)$ is the survival to age $(a)$, $m(a)$ is the fecundity schedule at age $a$ and $r$ is the intrinsic rate of increase, Hamilton (1966) formalized this idea by showing, theoretically, how individual fitness (measured as the intrinsic rate of increase) could be affected by changes in the age-specific fertility and survival schedules. Hamilton showed that the force of selection acting on survival $l(a)$ declines with age, reaching zero at the end of reproduction, just as predicted by Medawar. Similarly, Hamilton (1966) also showed how natural selection can attenuate fertility $m(a)$ with age, leading to a decline in fertility

before the onset of reproduction. More recently, more inclusive models of mutation accumulation have been developed, which combine genetic effects of age-specific changes to predict how means and variances in mortality schedules are influenced by deleterious mutations (Charlesworth 2001). Understanding whether these age-specific mutations act additively or proportionally is an unresolved issue but has important implications for the effects of mutation accumulation and senescence (Baudisch 2005).

An alternative theory for the evolution of longevity, *antagonistic pleiotropy*, proposed by Williams (1957) suggests that there is a trade-off between early fecundity or survival and late mortality. Genes acting in a beneficial way to favour fecundity and survival have a detrimental effect late in life. A modification of the antagonistic pleiotropy theory predicts differential patterns of resource allocation between somatic and reproductive tissues (Kirkwood 1977; Kirkwood & Rose 1991). The *disposable soma* theory proposes that resources are required to maintain cell integrity and, as such, there is a trade-off in reproductive capacity and physiological integrity.

If the evolution of ageing is determined by mutation accumulation, then patterns of additive genetic variance for survival and fertility should increase with age (Partridge & Barton 1993). Testing this theory, Rose & Charlesworth (1980) showed that the genetic variance in female fecundity (measured as the number of eggs laid) in *D. melanogaster* was constant. As such, these results provide little support for the mutation accumulation theory. However, methodological issues associated with small sample sizes, genetic correlations and loss of genotypes (Partridge & Barton 1993; Bulmer 1994) are likely to influence the interpretation of these results. More rigorously, in support of the mutation accumulation theory, Hughes & Charlesworth (1994) have shown that genetic variance in mortality rate increases with age in male *D. melanogaster*. Similarly, using a more rigorous experimental design, Hughes *et al.* (2002) have shown that genetic variation in age-specific reproductive success and inbreeding effects increased with age in *D. melanogaster*. As predicted by the mutation accumulation theory these late-onset genes with deleterious effects are not purged by natural selection (Hughes *et al.* 2002) and provide strong support for the mutation accumulation theory.

Tests of the antagonistic pleiotropy theory have used artificial selection experiments (rather than studies based on standing genetic variance) on *Drosophila*. By selecting lines for late reproductive output, it has been shown, in general, that there is a trade-off: longevity and late fertility increase from lines initiated from 'old' adults (Rose & Charlesworth 1980) and there is a correlated decline in survival and fertility of 'young' adults (Rose 1984; Partridge & Fowler 1992).

More recently, tests on the evolutionary theories of ageing have been more broadly interpreted and studies have aimed to separate non-adaptive and adaptive hypotheses (Keller & Genoud 1997; Reznick *et al.* 2004). It is postulated that the rate of ageing should increase, reproduction should start early and average lifespan decline as the rate of extrinsic mortality increases. Keller & Genoud (1997) demonstrated that variation in ant lifespan correlates with variation in extrinsic mortality: ants with long lifespans suffer low levels of extrinsic mortality (probably due to the evolution of complex eusociality). Most recently, Reznick *et al.* (2004) have suggested that a straightforward relationship between extrinsic mortality and longevity may be too simplistic and a more pluralistic approach to the evolution of longevity is necessary. Using guppies, *Poecilia reticulata*, Reznick and colleagues showed that fish derived from different (high and low) mortality environments and reared at two different levels of resource availability showed different patterns in lifespan. Guppies from high-mortality environments began reproducing earlier, suffered significant decline in neuromuscular function but tended to have longer total lifespans. These differences suggest that physiological condition, function or structures may be of critical importance in the evolution of senescence.

Concomitantly, with the development of these theories and tests has been the appreciation that mortality rates are heterogeneous: within the same cohort some individuals age faster than others. Theories and tests of the evolution of longevity presume that patterns in mortality can be described by a simple Gompertz model (equation (2.1)), yet it is now widely accepted that mortality rate can change in a non-constant way (Strehler & Mildvan 1960) and may decline or plateau in late-life (Carey *et al.* 1992; Curtsinger *et al.* 1992; Vaupel *et al.* 1994, 1998, 2004). Attempts to explain these patterns have focused on the pleiotropic action of genes (Mueller & Rose 1996; Charlesworth & Partridge 1997), the consequences of size (Vaupel *et al.* 2004) or physiological structure (Mangel & Bonsall 2004), or as compounded stochastic processes (Rose & Mueller 2000; Weitz & Fraser 2001; Mangel 2002).

Given the variability in the manifestations of the molecular mechanisms of ageing, it is, however, entirely plausible that different patterns in mortality trajectories might arise through an interaction between genetic and environmental processes. Gene by environment interactions occur when different genotypes respond to different environments in unique ways (Via 1984; Via & Lande 1985; Lynch & Walsh 1998). For example, Clare & Luckinbill (1985) showed that selection for increased and decreased longevity in *D. melanogaster* led to differing responses in environments of high and low larval competition. In highly competitive environments, genes acted in an additive manner and the lifespan of hybrid phenotypes was intermediate between long- and short-lived flies. In less competitive environments, genes for short-lifespan were dominant (Clare & Luckinbill 1985). To illustrate how gene by environment interactions might affect the patterns and trajectory of mortality, consider the scenario where intrinsic mortality is influenced by a gene by environment interaction. This could be defined as a simple extension of the Gompertz model (equation (2.1))

$$\mu(a) = A + C\exp(Ga) + \exp(Ga)\mathrm{f}(E), \tag{2.3}$$

where $C\exp(Ga)\mathrm{f}(E)$ is the gene ($C\exp(Ga)$) by environment ($\mathrm{f}(E)$) interaction. Illustrations of how

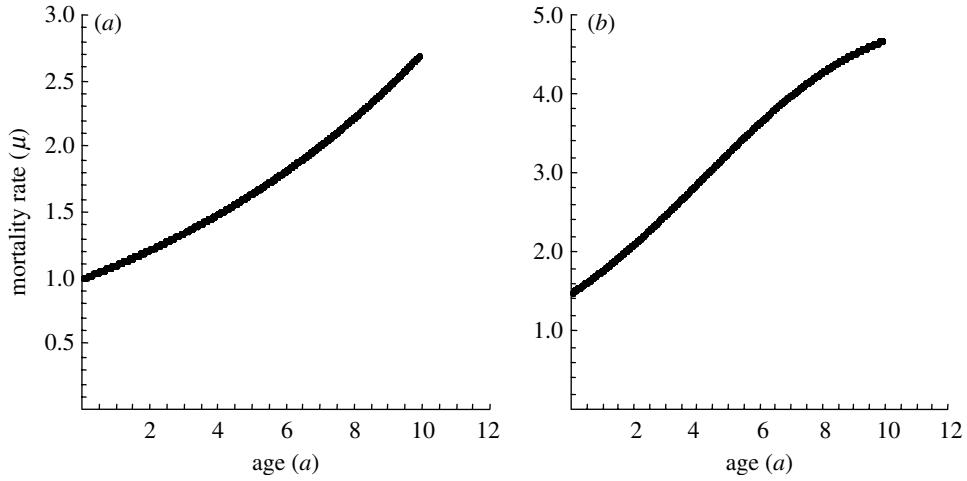


Figure 2. The effects of gene by environment interactions on mortality trajectories. (*a*) no gene by environment interaction, mortality follows a Gompertz model. (*b*) with a gene by environment interaction, mortality rate changes in a non-constant way. It is assumed that the effects of the environment (described as a measure of variability ($\sigma$)) operate around the age at maturity ($t(a)$) and the effects are distributed according to $\exp(-1/2((t-t(a))/\sigma)^2)$.

gene by environment interactions can affect the instantaneous death rate ($\mu(a)$) are shown in figure 2. As these mortality functions determine the probability of surviving to a particular age [$l(a)$] it would be interesting to develop this idea, and examine the fitness consequences of gene by environment interactions acting on mortality by incorporating such survival schedules into a life-history framework model (e.g. equation (2.2)). Gene by environment interactions suggests that plasticity or local adaptation underpin the magnitude and direction of the phenotypic response. Evaluating the effects of such interactions on life-history evolution necessitates the integration of the mechanistic studies of ageing together with an appropriate theoretical genetic framework. While there are numerous mechanistic studies on the processes of ageing, it is critically important that these proximate mechanisms elucidate the evolutionary theories.

### (c) *Evolutionary demography*

In an ideal world our iconic Darwinian demon would predominate. Organisms, however, must compromise and trade off life-history traits. Given these constraints, what are the trade-offs? How are they manifest? And what are the consequences for evolution (Bonsall *et al.* 2004). The principal approach for investigating such questions is through life-history theory (Cole 1954; Gadgil & Bossert 1970). The Euler–Lotka equation (equation (2.2)) is the fundamental way to look at how differing life-history decisions and trade-offs affect fitness, and ultimately evolution (Charlesworth 1994). Cole (1954) introduced the idea of exploring the outcome of selection by systematically studying the effect of changes in survival ($l(a)$) and fecundity ($m(a)$) on maximizing some measure of fitness (asymptotic growth rate, intrinsic rate of increase). This approach has had widespread appeal (Stearns 1992; Charlesworth 1994) and has led to a detailed theoretical basis for the evolution of a variety of life-history processes including the evolution of age at maturity, the evolution of semelparity (breeding once before dying) versus iteroparity (breeding many times before dying), kin selection and reproductive effort. Encompassing all of these is the evolution of senescence. Longevity is a trait that shapes demography and is shaped by evolution, and understanding how different life-history trade-offs affect the evolution of longevity is more inclusive than simply considering life table birth and death rates.

In appreciating that longevity is an adaptive trait shaping individual life histories, it is important to appreciate the subtleties involved. For instance, minor changes in environmental conditions can have extraordinary effects on life histories. Compensatory growth, the process whereby organisms recover from resource deprivation through catch-up growth, can have immediate ecological and long-term physiological and cellular costs (Metcalfe & Monaghan 2001). In the long term, costs of compensatory growth are likely to influence individual fitness through changes in fertility and survival schedules. However, their consequences for evolutionary demography and the evolution of longevity remain relatively unexplored. Similarly, accurately measuring schedules of age-dependent fertility and mortality is critical in the evolutionary demography of longevity (Partridge & Barton 1996; Minois *et al.* 2005). Recently, it has been shown that measures of age-specific mortality in plantain (*Plantago lanceolata*) depend on both fixed genetic characteristics and variable ecological and life-history factors such as temperature, rainfall and body size (Roach & Gampe 2004). Again, the consequences of more inclusive measures for age-specific life-history schedules (those including ecological and genetic factors) for the evolution of longevity remain unexplored.

The life history of an individual is determined by a set of constrained trade-offs (relationships defining the range and form of possible phenotypes). Natural selection operates to maximize fitness and precise trade-off combinations or values are selected based on their contribution to fitness. Exploring how trade-offs shape the evolution of longevity necessitates an understanding of how resources are allocated. Based on the antagonistic pleiotropy and disposable soma theories, Cichoń (1997), for example, developed a framework for exploring how growth, reproduction and repair affect variation in optimal resource allocation to influence patterns of longevity. Resource allocation

patterns are age-dependent: investment in maintaining somatic tissues is expected to be high early in life. The allocation of resources might also be shaped by extrinsic mortality rate and the effectiveness of repair: optimal allocation strategies are determined by the levels of mortality (Cichoń 1997). If extrinsic mortality risk is high, less resource is allocated to repair (and more to growth), the greater the degree of intrinsic mortality (cellular damage) and the lower the probability of surviving to a given age (Cichoń & Kozlowski 2000). Faster growth may promote early reproduction but occurs at the expense of resistance to mortality (Metcalf 2005). Such trade-offs (between growth and survival) shape evolutionary demography. In monocarpic plants (plants that flower once, set seed and die) such as *Carlina vulgaris*, *Cirsium vulgare* and *Cynoglossum officinale*, trade-offs between growth and survival determine the patterns of reproduction (Metcalf *et al.* 2003). Other studies (Cichoń 2001; Kindlmann *et al.* 2001; Novoseltsev *et al.* 2003) have suggested that the patterns of resource allocation affect age-dependent strategies of reproduction. Given that the onset of reproduction is a principal process in determining the evolution of longevity, appropriately interpreting these allocation strategies and the life-history consequences is vital.

Even though demographic patterns influence how longevity strategies might evolve, they also illustrate the remarkable levels of diversity and variation that can exist both within and between species. Explanations of maintenance in variation often rely on frequency-dependent selection or mutation-selection balance. However, complex patterns in trade-offs can give rise to flat or broadly equivalent fitness landscapes that maintain life-history variation. For instance, Mangel & Stamps (2001) have shown how trade-offs between growth and mortality can lead to the maintenance of individual variation in growth rate (through equivalent fitness). More recently, it has been shown how variability in mortality rates can be generated and maintained through life-history trade-offs and broad, flat fitness surfaces (Bonsall & Mangel 2004).

Adaptive responses to different environments are constrained not only by genetic architecture but are also limited by physiological mechanisms (Ricklefs & Wikelski 2002). Organisms will be constrained by their life histories; different life-history trade-offs will allow different fitness surfaces to be explored and might allow organisms with different characteristics to co-occur and diversify. We explore these consequences in more detail next.

## 3. PHYSIOLOGICAL STRUCTURE AND THE EVOLUTION OF LONGEVITY

The role of physiological structure and the evolution of demographic traits are inextricably linked. We examine this hypothesis here. Although there is a growing interest in the role of physiology in evolution (Ricklefs & Wikelski 2002; Bonsall & Mangel 2004; Mangel & Bonsall 2004), it is not new and has a long precedent. In the nineteenth century, T. H. Huxley commented that differences in physiology provide overwhelming support for the theory of evolution by descent through modification (see Darwin 1859). It is widely appreciated that differences in physiology affect the dynamics of population and determine the constraints on the evolutionary dynamics of life history (Mangel & Clark 1988; Houston *et al.* 1988; Clark & Mangel 2000). From an ecological perspective, we are interested in how life-history traits effect changes in population size through time. From an evolutionary perspective, we are interested in how and why traits under selection evolve.

### (a) *Population dynamics*

Individual mortality is the product of natural selection acting on behaviour, growth and reproduction, and of the physiological processes acting across the life of an organism. The physiological realities of longevity are that the metabolic processes associated with somatic growth and development (throughout life) are linked and that these processes are costly (Metcalfe & Monaghan 2001; Lummaa & Clutton-Brock 2002; see §2).

Although experiments have been used to explore how physiological attributes can affect longevity at the individual level (e.g. Service 1987; Djawdan *et al.* 1996), understanding how physiological factors affect the evolutionary dynamics of longevity requires an appreciation of the consequences of these life-history traits on the dynamics at the population-level. Changes in population size ($\Delta N$) can be generally expressed as

$$\Delta N = b(t) - d(t) + i(t) - e(t), \tag{3.1}$$

where $b(t)$, $d(t)$, $i(t)$ and $e(t)$ are the numbers of births, deaths, immigrants and emigrants at time $t$, and account for the proximate effects of a range of different ecological and physiological factors. It is now widely appreciated that physiological structures and processes affect the dynamics and interactions between populations (e.g. Metz & Diekmann 1986; Łomnicki 1988; Kooijman 1993).

For example, changes in the population dynamics of *Drosophila subobscura* (figure 3), a ubiquitous fruitfly that feeds on decaying and fermenting fruit, are principally determined by changes in mortality rate ($d(t)$; see electronic supplementary material). These changes in mortality operate in a density-dependent manner such that there is higher mortality at higher population sizes and lower mortality at lower population sizes. These patterns of mortality lead to populations that appear relatively stable (no wide fluctuations in numbers) through time (figure 3). Higher mortality rates at higher population sizes are completely consistent with the biology and mechanisms of ageing: intense competition for limiting resources, rapid development and sustained metabolic damage are more likely to be manifest when population sizes are large.

Nevertheless, when controlling for population size, cohorts of individuals show wide variation (Gavrilov & Gavrilova 1991) or heterogeneous distributions of mortality (figure 4): some individuals die young, while some individuals live to very old ages. Again, this remains consistent with the biology and mechanisms of ageing, where metabolic, cellular and physiological (genetic) differences exist among individuals.

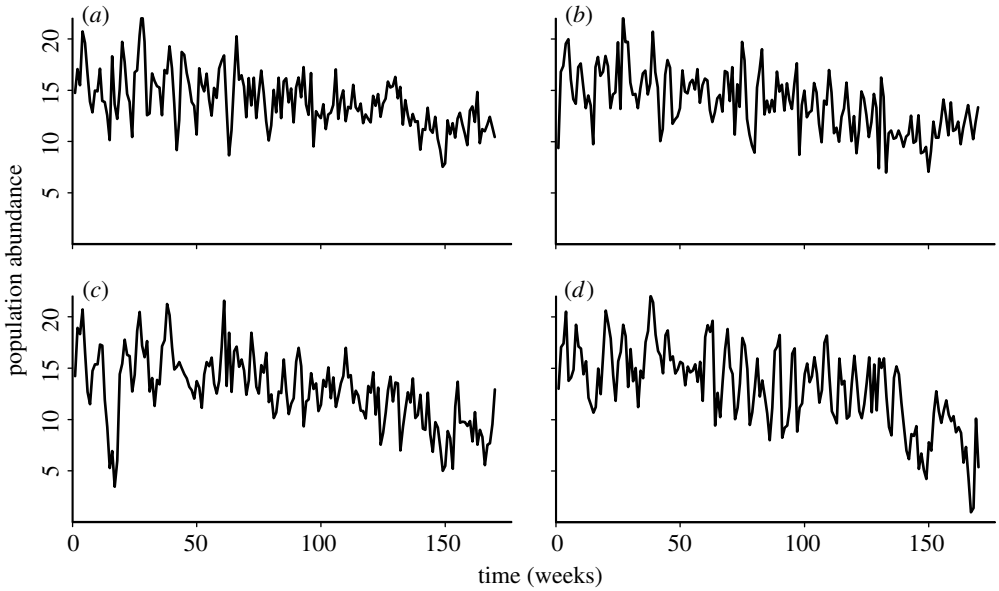


Figure 3. The population dynamics of *Drosophila subobscura*. Statistical analysis of the time-series reveals that the population dynamics (change in population size measured as weekly counts of abundance) are determined by changes in the adult mortality rate. Different functions for the birth and death rates were fitted to the time-series data. The best descriptor of these population dynamics is a model that includes a time-delayed density-dependent mortality function (see electronic supplementary material for more details).

Statistically, it is more appropriate to describe these patterns of longevities using a distribution with a non-constant hazard function (such as a Gamma: figure 4) as opposed to an Exponential distribution (which has a constant hazard function). Distributions with non-constant hazard functions (such as a Gamma) might arise naturally from a description of the waiting times between events (points of failure) that are Poisson (discrete random) distributed. Other non-random distributions have also been proposed to describe how mortality changes in a non-constant way with age (e.g. Gavrilov & Gavrilova 1991). Non-constant hazards of mortality have important consequences for the evolutionary dynamics of longevity.

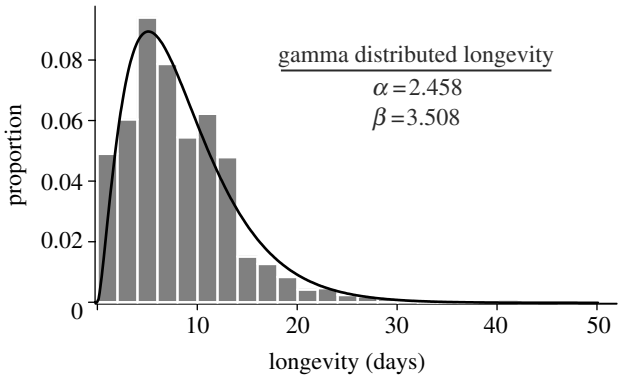


Figure 4. Gamma distributed longevity for *Drosophila subobscura*. Time to death for individually reared flies was recorded and different statistical distributions fitted. The best description of this pattern of mortality was a Gamma (fitted solid line), rather than an Exponential distribution, suggesting heterogeneity in fly mortality rate. The maximum likelihood parameters for the Gamma distribution were $\alpha = 2.458$ and $\beta = 3.508$.

### (b) *Evolutionary dynamics*

To explore the evolutionary consequences of physiological structure on longevity, it is necessary to define a measure of evolutionary change. This is often the fitness function of a rare mutant strategy. There has been controversy over the most appropriate measure for fitness (Hamilton 1966; Metz *et al.* 1992; Charlesworth 1994). In this paper, as is most often the case, when considering the effects of population dynamics and the evolutionary processes of mutation and selection, fitness is expressed in terms of the *per capita* population growth rate. This fitness function is used to determine the evolutionary stable states: when the rate of change of fitness is zero (Maynard-Smith 1982). Fitness functions also allow the broad dynamics of invasion and replacement to be examined. The structure and details of the model for analysing the evolutionary dynamics of the consequences of physiological structure on longevity are outlined in the electronic supplementary material.

The evolutionary outcome of (an initially rare) mutant strategy (a species with a different life-history trait to the resident) invading an environment where a resident is established is explored. Understanding how the fitness function of this invading mutant changes with changes in the life-history trait is the goal. The fitness function for changes in natural mortality rate ($\mu$) through time is illustrated in figure 5. This fitness surface or landscape reveals a number of features and predictions about the evolutionary response to changes in longevity.

Fitness of the mutant depends on what the resident strategy is doing: the response is frequency-dependent. Mutant fitness changes through time depending on how the resident's life-history trait is influenced by its physiology, and how this scales up from the individual to affect the population dynamics.

Depending on the population dynamics, we can identify a number of different evolutionary stable states, where the gradient of the fitness function is

zero (figure 5). For example, initially when the resident population size is small, there are a number of evolutionary stable states. Two of these points are fitness maxima (where $\mu = 1.65$ or where $\mu = \infty$) and the other is a fitness minima (where $\mu = 0.5$). When the resident population size has reached a stable or asymptotic state, we can identify only a single fitness maximum (where $\mu \to \infty$). Each of these evolutionary states provides predictions on the consequences of selection. The fitness minimum is a flat part of the surface and this could allow several similar strategies to co-occur. Selection around this point is likely to be disruptive and could promote phenotypic divergence. Such divergence could allow the emergence of strategies where species evolve to be more long lived (decline in $\mu$) or, conversely, species evolve to be shorter-lived (increase in $\mu$). However, it is entirely plausible that a branching occurs and phenotypes of both increased and decreased longevity emerge. Similarly, the fitness maximum is a broad part of the surface (across traits and through time). It is likely that selection around the fitness maximum will have a stabilizing influence on sets of species with shorter-lived phenotypes.

If a species has a relatively complex physiology, under what conditions will longer-lived species invade? And what, if any, are the evolutionary dynamic consequences of this? The invasion and replacement dynamics determine whether a rare mutant with a different set of life-history characters (than resident strategies) can invade and outcompete these existing strategies (again, details of the analyses for this part are confined to the electronic supplementary material).

The pairwise invasion boundaries and regions of coexistence for species with different life-history trait values are illustrated in figure 6. Invasion is successful for the one of the strategies (say the mutant) above the grey line and, conversely, invasion is successful for the other strategy (say the resident) to the right of the black line. The lines are zero-growth isoclines and denote precisely where fitness for each of the strategies is exactly zero. Fitness (*per capita* growth rate) is zero for both strategies at the point where the two lines intersect. The shaded wedge in figure 6 illustrates the frequency-dependent, asymptotic conditions under which a longer-lived strategy will invade. However, it is predicted that invasion and replacement of strategies will be more likely to occur between individuals which are relatively short-lived (larger $\mu$). In fact, it is expected that over a broad range of life-history combinations strategies may co-occur rather than exclude one another.

Numerical solutions of the model (see electronic supplementary material) show how coexistence of species with different physiological complexities might occur through mutation and strategy replacement. Of particular interest is whether several different strategies can co-occur, how different these strategies are and how long they persist. As predicted from the fitness and invasion analyses, it is possible for multiple species to co-occur (figure 7) provided there is sufficient difference in their life histories (Bonsall & Mangel 2004; Bonsall *et al*. 2004). Within these assemblages, strategies with different physiological complexities may persist as long transients, and the number that coexist at any point in time might exceed the number observed in the terminal assemblage. Different coexisting strategies give rise to different mortality trajectories (figure 7), where differences in physiological complexity lead to distributed or heterogeneous mortality trajectories. The evolution of heterogeneity in mortality trajectories is linked to physiological complexity. It is obvious that it is possible to speculate on the cellular and molecular mechanisms which might result in increased physiological complexity (e.g. ability to deal with oxidative damage) and allow the evolution of heterogeneous mortality trajectories. However, without modelling specific damage and repair mechanisms (e.g. Mangel & Bonsall 2004) it is only prudent to reflect that the diversity of heterogeneous mortality patterns reflects the diversity of observable strategies (Pearl & Miner 1935). Given these predictions and the variety of different molecular mechanisms by which heterogeneous mortality trajectories might evolve, it seems somewhat injudicious to seek out characteristics, biomarkers or behaviours that might be predictors of longevity. More challenging, with higher rewards, is understanding the mechanisms, sources and roles of heterogeneity in natural populations (Partridge & Mangel 1999) and combining this with a more robust evolutionary (as opposed to a biodemographic) approach to longevity life-history theories.

## 4. FUTURE PERSPECTIVES

### (a) *Resource provisioning and longevity*

#### (i) *What is the effect of differential resource provisioning on longevity?*

Deciding on the patterns of resource provisioning of offspring has important ecological (storage effect: Warner & Chesson 1985) and evolutionary (bet-hedging: Cohen 1966) implications. For example, recent empirical evidence on black rockfish (*Sebastes melanops*) has revealed how patterns of maternal investment are important determinants of larval fish growth and survival (Berkeley *et al*. 2004). In particular, this study showed how progeny from older fish were far better provisioned with more energy-rich triacylglycerol lipids than progeny from younger fish. More resource leads to faster growth and increased survival and it has been suggested that small differences in growth rate can impact on survival and longevity (Berkeley *et al*. 2004).

A corollary of maternal investment is the conflict that arises between parents and offspring in the allocation and acquisition of resources (Trivers 1974). If there is parental investment in offspring, then significant and often lethal conflict can occur among siblings, despite the close degree of genetic relatedness. In sexually reproducing species, parents contribute 50% of their genes to offspring. Each offspring receives a different 50% from each parent, so at best, offspring are related by 1/2. Differential fitness interests are then expected to exist between both parents and offspring and among siblings (Mock & Parker 1997).

The conventional theory of ageing (Medawar 1952; Hamilton 1966) explains why mortality increases with age: continued survival contributes less to reproductive

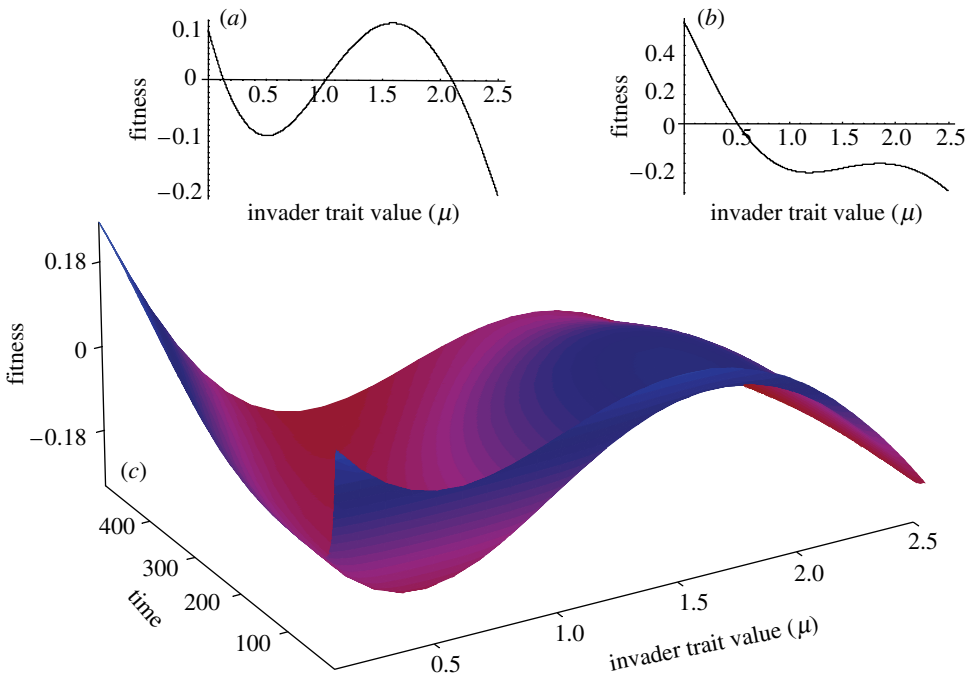


Figure 5. Fitness surface for changes in invader natural mortality rate ($\mu_i$) as a function of time. This fitness surface shows that the optimal response depends on how mortality is distributed and cascades through the life cycle of the resident strategy. The response is frequency-dependent and can lead to a variety of effects: either a combination of long-lived and short-lived strategies are expected to arise (two fitness peaks; $t=100$) or only long-lived strategies are expected to persist (have maximum fitness benefits; $t=500$). Inserts show these snapshots of the fitness surface at (*a*) $t=100$ and (*b*) $t=500$.

fitness after maturity. However, successful reproduction may involve a variety of resource provisioning processes, such as the role of inter-generational transfers of resources (Lee 2003; Lahdenpera *et al.* 2004) and the potential conflict between siblings. The conventional theories of longevity do not consider how patterns of resource transfer might impact the evolution of senescence.

Appreciating how life-history traits are influenced by differences in resource allocation rules has only recently been considered. While it has been widely appreciated that transfer of resources from individuals beyond the age of maturity is an important contribution to individual fitness (Medawar 1952; Hamilton 1966), formal theories of resource transfer patterns on ageing are scarce. Lee (2003), for example, has combined selection due to transfers across the lifespan of an organism with the conventional theory of selection acting on fertility. Using an age-structured model that incorporates population size and inter-generational transfers, Lee (2003) showed how increasing fitness (measured as population growth rate *r*) increments can be achieved by differential resource production, utilization and transfer. Recent empirical evidence provides some support for the role of resource transfers in influencing patterns of ageing. Resource provisioning of honeybee workers with protein-rich vitogellein can modulate patterns in longevity and allow worker bees to over-winter (Amdam & Omholt 2002). Moreover, the patterns of age- and stage-dependent food transfers are important in affecting caste function and ageing (Amdam & Page, 2005). However, more broader evolutionary aspects of resource allocation patterns and trade-offs might have appreciable effects on the evolution of longevity. For example, it remains

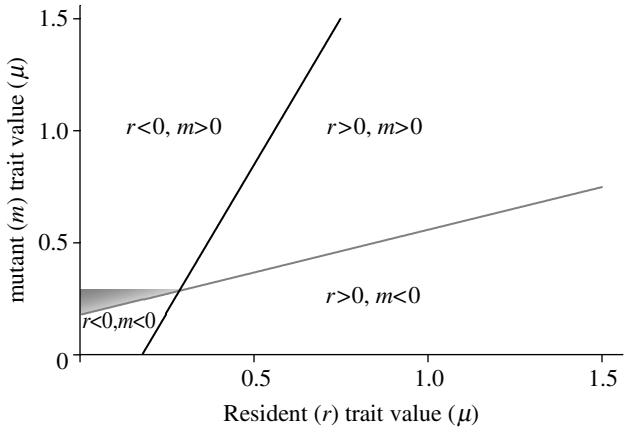


Figure 6. Reciprocal invasion boundaries for two competing strategies (resident *r* and mutant *m* strategies) with relatively complex physiologies (ability to deal with damage). Invasion is successful for the mutant (*m*) strategy above the grey line and for the resident (*r*) strategy to the right of the black line. The shaded wedge represents the strategies where a long-lived mutant would invade and exclude the resident. The region ($r>0$, $m>0$) denotes an area of coexistence between the resident and the mutant strategies. Here, it is predicted that both long and short-lived strategies will co-occur (see electronic supplementary material for details about the model).

unresolved how the conflict between parents and offspring and differential pre and post-natal investment affects the evolution of longevity.

### (b) *Population genetics of ageing*

#### (i) *Does genome size, integrity or complexity determine lifespan?*

Interspecific species differences in longevity are related to the patterns of genome and tissue maintenance, damage and repair. Recent studies have suggested that

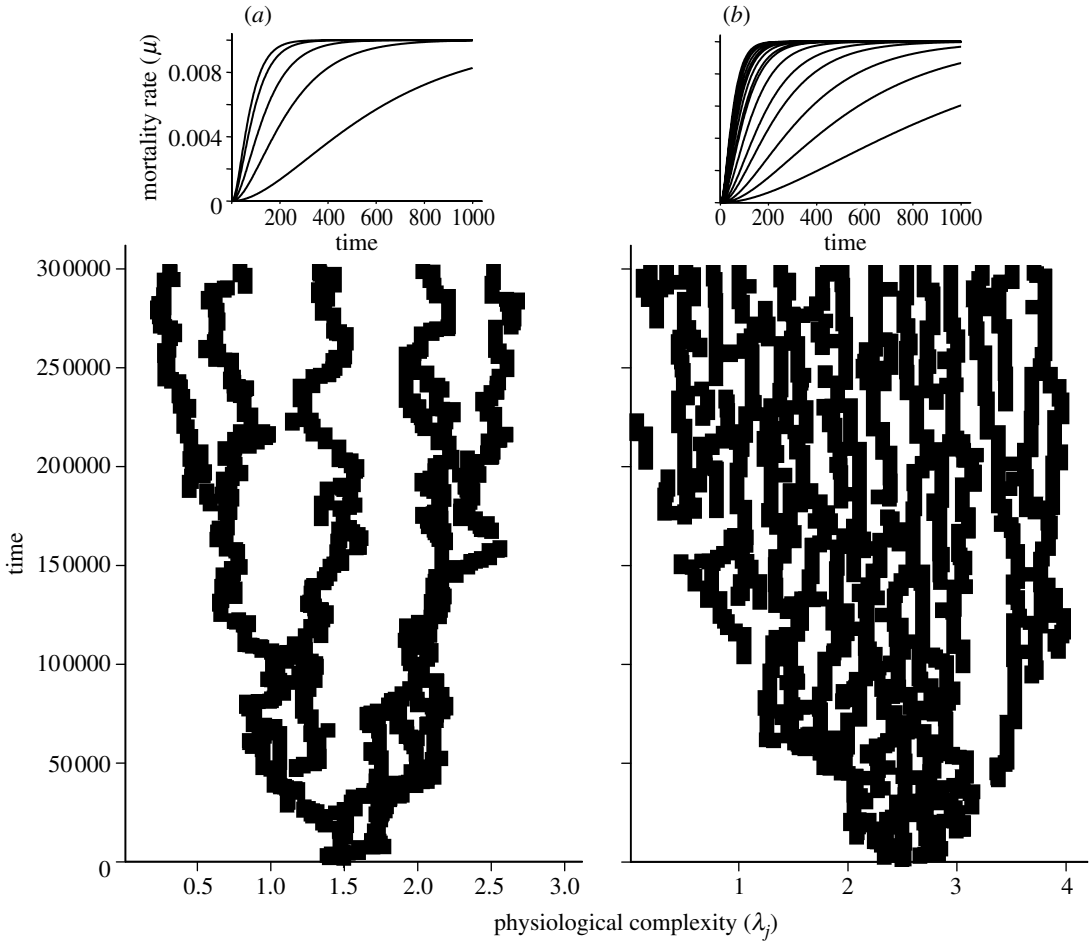


Figure 7. Evolutionary dynamics and coexistence of strategies with different life histories (physiological complexities; $\lambda_j$). The evolution of physiological complexity governs how mortality cascades through the life cycle of the strategy. High $\lambda_j$ is indicative of the rapid progression of 'damage' leading to rapid mortality while low $\lambda_j$ suggests an increased ability to deal with 'damage'. Branching processes are illustrated for different rates of physiological innovation: (*a*) low physiological innovation ($\sigma_\nu = 0.05$) and (*b*) high rates of physiological innovation ($\sigma_\nu = 0.1$). Inserts show the different heterogeneous mortality rates that evolve between strategies in the terminal assemblages (see electronic supplementary material for details about the model).

there might be a link between genome size and lifespan (Monaghan & Metcalfe 2000; Griffith *et al.* 2003) which, given our understanding of the molecular machinery of ageing, is entirely plausible. For example, in birds, a significant positive relationship exists between genome size and longevity (when corrected for body size; Monaghan & Metcalfe 2000). Similarly, a comparative analysis of different fish orders with well resolved phylogenetic relationships also shows a positive relationship between genome size and longevity (Griffith *et al.* 2003). Even though such relationships may depend on the measure of longevity used (Morand & Ricklefs 2001) or statistical methodology (Gregory 2004), it is evident that the genome complexity can impose strict physiological constraints on life histories (Gregory 2002).

Although the precise causal link between genome size and longevity remains unresolved, it has been suggested that alterations in DNA content could affect the period that cells spend in the different phases of the cell cycle (Gregory 2001): increase in genome size leads to slower cell growth. Notwithstanding, understanding changes in genome size (Monaghan & Metcalfe 2000) and gene function (Gems 2001; Tissenbaum & Guarente 2001) are likely to be important for the population genetics of ageing. Increases in genome size can occur through a number of chromosome and gene specific mechanisms such as polyploidy, chromosome rearrangement, inversions or gene duplication. Duplication of genes or genomes is thought to be one origin of material for the evolution of novel function, increased complexity and speciation (Holland *et al.* 1994; Lynch & Conery 2000).

Gene duplication, redundancy and specialization has attracted recent attention and has a number of population genetic consequences (Nowak *et al.* 1997; Lynch & Force 2000; Lynch *et al.* 2001), but most interestingly (from an evolution of ageing perspective) might eliminate the pleiotropic constraints unique to single-copy genes. Genes often have several functions each controlled by different regulatory mechanisms with multiple pleiotropic effects. Redundancy or specialization can take a number of distinct forms such that the expression of gene duplicates occurs in different tissues or in novel developmental stages (Force *et al.* 1999). As noted, one of the central themes in the evolutionary biology of longevity is the idea of antagonistic pleiotropy (Williams 1957). While gene-duplication and specialization does not contradict this theory, developing a population genetic framework to explore how genome size and gene duplications might affect the patterns and predictions on longevity

evolution will refine the evolutionary theory of ageing. For example, it is reasonable to ask how important are stochastic mechanisms, such as random drift, in maintaining variability on which selection for increased longevity can operate? Resolving these problems will require a more in-depth appreciation of the molecular machinery of ageing, the pleiotropic effects of mutations and a theoretical framework linking gene duplication and life-history theory.

### (c) *Comparative biology of ageing*

(i) *How do geographic patterns in longevity within species affect diversification and diversity?*

The rockfishes (*Sebastes* spp.) are known to show marked variability in patterns of lifespan (figure 1*b*); understanding how such assemblages are structured requires the novel integration of life-history theory, population dynamics and comparative biology. While recent findings (Bonsall & Mangel 2004; Bonsall *et al.* 2004), together with the results presented here, suggest that ecological communities and guilds can be structured by differences in life histories, geographic variation within a species is a central theme to the origin of new species. Natural selection operating on life-history characteristics is clearly of overwhelming importance in generating and maintaining within species variability (see §2*c*). While it is evident that variability in longevity exists in populations and that this is linked to reproductive output (Partridge & Farquhar 1981), the effects of geographic variability in longevity within a species remains rarely explored. While some steps to reconciling this work have been achieved (Reznick *et al.* 2001; Bonduriansky & Brassil 2002), tests on populations derived from geographically distinct places remain rare. Developing an appropriate comparative study of life-history traits within a species remains a novel area for investigating life-history traits such as the evolution of longevity.

The dynamics of populations interplay with evolution to shape variation in life-history traits. Developing tests of these ideas and theory is another compelling theme in investigating how longevity shapes demography and is shaped by evolution. Can differences in the dynamical regimes experienced by populations affect the evolutionary trajectories, strength of selection and life-history trade-offs? A number of empirical systems (such as bacteria, flies and fish assemblages) might be appropriate for developing such evolutionary experiments and with a broad remit of integrating ecological and evolutionary dynamics. This potential research area is intriguing, realistic and challenging.

In concert, developing comparative studies of longevity traits among species will provide evidence of whether these life-history traits are capable of affecting demography and structuring species guilds and assemblages. Again, while there is some evidence to suggest that senescence is highest in short-lived species (Promislow 1991), appropriately developed comparative biology tests of highly variable life-history traits remain undeveloped.

## 5. CONCLUSIONS

Ageing is a deleterious trait. In some respects this is a conventional evolutionary puzzle, in others it is not. Understanding why and how fertility and survival decline through time should be a relatively straightforward problem. However, the multitude of mechanisms by which ageing and senescence occur leaves a bewildering array of potential explanations for the longevity problem. Without evolutionary theories, these deleterious effects of the molecular manifestations of ageing remain just that, as manifestations rather than paths to elucidating the puzzle. Our goal in developing an evolutionary theory of longevity and ageing should be to capture, in a biologically realistic way, the observed patterns of age-specific survival, fertility and growth. The aims of this article have been to highlight how the theory of longevity has developed and where progress towards this goal could be focused. One possible resolution, as mentioned, is describing how non-constant mortality trajectories fit with the quantitative genetics of ageing. Developing a cohesive theory on the population biology (genetics, ecology) of longevity is necessary, since without it there is no guidance or interpretation for understanding the diversity of the molecular machinery. While the mechanisms of ageing cannot be pinned onto a single gene, the molecular manifestations of cellular damage and replication all have evolutionary consequences in terms of pleiotropy and mutation accumulation. It is timely to revise the evidence we have before us and appreciate the reasons for the evolution of ageing. Darwin advocated a deductive over a cumulative approach for understanding the origin of species (Darwin 1859). If we believe our philosophy of science (Kuhn 1996), then having an appropriate evidence-based paradigm to work within provides the necessary epistemological framework for developing a realistic theory of why we grow old. Only by working with this framework can we shatter that iconic Darwinian demon.

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